REMARKS

Attorney Docket No.

Please note that the attorney docket number for this matter has changed to 402076.

The Claim Amendments

Claims 26-30 and 34-38 are amended to more particularly describe the claimed aspects of Applicants' invention. Most of the claim amendments are directed to improving the form and readability of the claims (e.g., replacing "said" with "the," adding the referent "a" with respect to particular elements to provide antecedent basis, etc.). Independent claims 26, 29, and 37 are amended so as to read on taxane preconcentrates comprising a carrier system or composition that includes (1) a surfactant component consisting of one or more non-ionic surfactants and (2) a hydrophilic component in an amount up to 40% w/w of the carrier system or composition.

New claims 39-53 are directed to additional novel, nonobvious, and useful aspects of the Applicants' invention. For example, claims 42, 45, and 51 are directed to taxane preconcentrates comprising a carrier system that has a hydrophilic component that is at least in part ethanol, such that the carrier system contains at least 6% w/w ethanol, claims 46 and 51 are directed to preconcentrates having a surfactant component consisting of particular surfactants or combinations of surfactants, and claim 53 is directed to a pharmaceutically acceptable composition comprising a taxane preconcentrate according to another particular aspect of the invention.

The use of the phrases "one or more" and "at least one" in the amended and new claims, for example with respect to the non-ionic surfactant element in some claims, does not imply that the use of the referent "a" with respect to other claim elements restricts these claim elements to the singular. Thus, for example, it will be understood that "a hydrophobic component" can include more than one hydrophobic component, in accordance with regular U.S. patent practice.

The claim amendments and new claims are supported by the originally filed specification and claims. Specifically, for example, the amendments to claims 26, 29, and 37, with respect to the non-ionic surfactant component(s) of the carrier system or composition find support at, e.g., page 4, lines 4-7 and lines 12-13; page 5, lines 16-22; page 7, lines 16-28; and original claims 1 and 2. As noted above, these claims also are amended to specify that the carrier or composition possesses some amount of a hydrophilic component (i.e., these claims are

directed to preconcentrates having a carrier or composition including "up to 40% w/w" of a hydrophilic component, as opposed to "0-40% w/w" of such a component). Support for this aspect of the claim amendments is found throughout the specification, including, e.g., the passages at page 4, lines 4-7; page 5, lines 16-19; page 6, lines 6-7; and original claims 1-2.

New claims 39 and 50 are supported by, e.g., the disclosure at page 4, lines 12-13 and page 4, line 19 - page 5, line 15 and the aforementioned sections and claims referenced with respect to the amendments to claims 26, 29, and 37. The subject matter of new claims 40, 44, 47, and 50 find additional support (besides the aforementioned claims and passages) in original claim 12. The subject matter of new claims 41, 48, and 52 finds support in, e.g., Example 6. The subject matter of new claims 42 and 45 find support at, e.g., page 4, lines 13-16; page 6, lines 25-29; page 7, lines 16-28; page 9, lines 11-22; and the aforementioned sections and claims. New claims 43 and 49 are supported by the disclosure at, e.g., page 7, lines 16-17 and 25-29. The subject matter of new claims 46 and 51 finds support in the aforementioned sections and claims, as well as at, e.g., page 4, lines 13-16 and page 6, lines 25-29. New claim 53 is supported by, e.g., original claim 18.

In view of the support found in the originally filed specification and claims, no new matter has been added by way of the claim amendments and new claims. Other amendments, not specifically addressed here, are similarly supported by the original claims and disclosure, or consist of nonsubstantive wording, style, and grammar changes.

Claims 26-53 are pending. Claims 26, 29, 37, 39, 45, 51, and 53 are independent claims. The precise amendments made to the claims are set forth in an attachment hereto. A set of the pending claims, as amended, also is attached hereto for the convenience of the Examiner.

The Office Action

The Office Action rejected claims 26-38 under 35 U.S.C. § 103 as allegedly obvious. Specifically, the Office Action rejected claims 26-33 and 36-38 as allegedly obvious in view of the combination of U.S. Patents 5,342,625 (Hauer et al.) and 5,929,030 (Hamied et al.), and optionally in further combination with U.S. Patent 6,004,573 (Rathi et al.). The Office Action rejected claims 34-35 as allegedly obvious in view of the combination of the Hauer '625 patent and the Hamied '030 patent, in view of International Patent Application WO 96/35415 (Sime et al.), and, optionally, in further view of the Rathi '573 patent.

The Pending Claims are Patentable Over the Cited References

The Office Action rejected all of the claims of the subject application as allegedly obvious in view of the Hauer '625 patent and the Hamied '030 patent, with optional further reference to the Rathi '573 patent. For the following reasons Applicants respectfully submit that the combination of the Hauer '625 patent and the Hamied '030 patent cannot support a *prima facie* obviousness rejection of the currently pending claims.

To establish a *prima facie* obviousness rejection against a claim, *all* of the elements of the claim at issue *must be taught or suggested by the cited references*. See, e.g., M.P.E.P. (8th Ed.) § 2143.03 (2001). A reference that teaches one of ordinary skill in the art away from the claimed invention cannot render the claimed invention unpatentably obvious. See, e.g., *Dow Chemical Co. v. American Cyanamid Co.*, 2 U.S.P.Q.2d 1350 (Fed. Cir. 1987). Moreover, a reference cannot be modified or combined with another reference to support a §103 rejection, where such modification or combination would change the principle of operation of the reference or render the cited reference unsuitable for its intended purpose. See, e.g., M.P.E.P. (8th Ed.) § 2143.01. If an independent claim is nonobvious under 35 U.S.C. § 103, any claim depending therefrom also is nonobvious. See, e.g., *In re Fine*, 5 U.S.P.Q.2d 1596 (Fed. Cir. 1988).

The Hauer '625 patent is directed to cyclosporin microemulsions. The Hauer '625 patent does not teach or suggest a preconcentrate of a taxane, much less the oral or parenteral administration of such a preconcentrate. Accordingly, the burden rests with the Office to identify references in the prior art that would have motivated one of ordinary skill in the art to modify the teachings of the Hauer '625 patent to arrive at the subject matter of the pending claims. In this respect, the Office Action relied on the Hamied '030 patent in combination with the Hauer '625 patent to reject independent claims 26, 29, and 37 under Section 103 (see Office Action at pages 2-3).

Claims 26, 29, and 37, as amended, and new independent claim 39, are directed to taxane preconcentrates that comprise a composition or carrier system that consists essentially of, among other things, a surfactant component that *consists* of one or more *non-ionic* surfactants. In contrast, the Hamied '030 patent is directed to microemulsions that desirably, if not necessarily, comprise a "mixture of lecithin and another surfactant," both of which, the Hamied '030 patent states, "are necessary to obtain the significant advantages of the invention." Col. 2,

lines 46-50 (see also col. 3, lines 43-43 and col. 3, lines 62-66). Lecithin is an ionic phospholipid surfactant. Accordingly, the Hamied '030 patent teaches *away from*, not towards, a preconcentrate comprising a carrier system or composition, which consists essentially of, among other components, a surfactant component that *consists* of one or more *non-ionic* surfactants. Therefore, the combination of these references cannot properly support a *prima facie* obviousness rejection against these claims. Besides teaching away from the present invention, such a combination of references requires an impermissible modification of the Hamied '030 patent. See M.P.E.P. § 2143.01, as mentioned *supra*. As the combination of the Hauer '625 and Hamied '030 patent cannot appropriately support a Section 103 rejection against claims 26, 29, and 37 a rejection of any claim that depends on one of these claims under Section 103, based on the cited combination, also would be misplaced. A similar analysis applies with respect to new independent claim 39, and new claims 40-44, which are dependent on this claim.

New claims 40, 42, and 44 are directed to taxane preconcentrates comprising a carrier system that consists essentially of a combination of components, one of which is a hydrophilic component formed at least in part by ethanol, such that at least 6% w/w of the carrier system consists of ethanol. The Hamied '030 patent explicitly *teaches away* from such taxane preconcentrates, repeatedly indicating that the presence of ethanol in the emulsions described therein is undesirable, if not totally excluded. For example, in one passage the Hamied '030 patent states:

> In the microemulsions of the invention, component (d) is a hydrophilic phase. The preferred material is propylene glycol, but other substances can be used. Ethanol cannot be present.

Col. 3, lines 49-52 (emphasis added); see also col. 1, lines 27-29 and col. 2, lines 8-19. Thus, the Hamied '030 patent also *teaches away from*, not towards, the subject matter of new independent claim 45; new claims 46-50, which depend on claim 45; new claims 51-53; and new claim 42. For this reason, and because the proposed combination with the Hauer '625 patent would improperly modify this central element of the Hamied '030 patent, the combination of these references cannot be properly be cited to establish a Section 103 rejection of these claims.

New independent claim 51 is further directed to a preconcentrate of a taxane in a composition *consisting essentially of* a mixture of components, including a surfactant

component, which *consists* of particular recited surfactants or combinations of such surfactants. The use of "consists" restricts the preconcentrate from other preconcentrates including other surfactants, including, e.g., lecithin. Accordingly, the Hamied '030 patent also teaches away from, not towards, such a taxane preconcentrate. Therefore, a Section 103 rejection of claim 51 or claim 52 (which depends on claim 51) based on the combination of the Hamied '030 patent and Hauer '625 patent would be misplaced.

Moreover, even if the combination of the Hauer '625 and Hamied '030 patents was permissible (which, as explained above, is not the case), such a combination of references would still fail to support a *prima facie* obviousness rejection against claims 26, 29, and 37, because the combination fails to teach or suggest all of the elements of these claims. For example, there is no teaching or suggestion in the proposed combination that a preconcentrate of a taxane in a microemulsion can provide a taxane bioavailability of 25 to 60% upon oral administration. Further in view of this unexpected and beneficial property of the claimed taxane preconcentrates, these claims, as well as claims that depend from these claims, would be patentable over such a combination.

The remaining rejections made by the Office Action, which cite the Rathi '573 patent and/or the Sime '415 application, rely on the proposed combination of the Hauer '625 patent and Hamied '030 patent (see pages 3 and 4 of the Office Action). As discussed above, the proposed combination of these primary patents is improper under Section 103 with respect to the pending claims. As such, whatever deficiencies in the proposed combination of the Hauer '625 and Hamied '030 patents that the Office Action sought to address by reference to the Rathi '573 patent and/or the Sime '415 application are moot in view of the fact that the proposed combination of references, which lies at the heart of such rejections, is not proper under Section 103 with respect to the pending claims.

Conclusion

The application is considered in good and proper form for allowance, and the Examiner is respectfully requested to pass this application to issue. If, in the opinion of the Examiner, a telephone conference would expedite the prosecution of the subject application, the Examiner is invited to call the undersigned attorney.

Respectfully submitted,

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Attorney Docket No. 402076 (*formerly* 121-160) PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:

Parikh et al.

Application No. 09/281,430

Filed: March 30, 1999

For: ANTICANCER COMPOSITIONS

Art Unit: 1615

Examiner: Ware, T.

AMENDMENTS TO THE CLAIMS
MADE IN RESPONSE TO OFFICE ACTION DATED JUNE 25, 2002

26. (Amended) A storage-stable, self-emulsifying, and non-aqueous~~,~~ preconcentrate of a taxane in a microemulsion comprising a ~~consisting essentially of said~~ taxane dissolved in a carrier system, which carrier system consists essentially of:

10 to 80% w/w of a hydrophobic component selected from the group consisting of a triglyceride, a diglyceride, a monoglyceride, a free fatty acid, a fatty acid ester, a fish oil, a vegetable oil, and combinations thereof;

20 to 80% w/w of a surfactant component ~~phase~~ consisting of ~~comprising at least~~ one or more non-ionic surfactants;

up to 35% ~~0-35%~~ w/w diethylene glycol monoethylether; and

up to ~~0 to~~ 40% w/w of a hydrophilic component selected from the group consisting of a hydroxyalkane, a dihydroxyalkane, a polyethylene glycol having an average molecular weight of at most 1000, and combinations thereof;

wherein the ~~said~~ preconcentrate, when mixed with ~~an aqueous medium selected from the group consisting of~~ water or simulated gastric fluid, gives an average droplet size of at most 10 microns~~;~~, and ~~which upon oral administration of~~ a dose of the preconcentrate has a taxane bioavailability of ~~ranging from~~ 25~~%~~ to 60% of the ~~said~~ taxane in the ~~said~~ dose upon oral administration.

27. (Amended) The self-emulsifying preconcentrate of claim 26, wherein the carrier system contains ~~containing from~~ 15 to 75% w/w of the hydrophobic component.

28. (Amended) The self-emulsifying preconcentrate of claim 26, wherein the carrier system contains ~~containing~~ up to 30% w/w of the hydrophilic component.

29. (Amended) A storage-stable, self-emulsifying, and non-aqueous~~, clear, liquid~~ preconcentrate of at least one taxane in a composition consisting essentially of:

10 to 80% w/w of a hydrophobic component selected from the group consisting of a triglyceride, a diglyceride, a monoglyceride, a free fatty acid, a fatty acid ester, a fish oil, a vegetable oil, and combinations thereof;

20 to 80% w/w of a surfactant component ~~phase~~ consisting of ~~comprising at least~~ one or more non-ionic ~~surfactant~~ surfactants; and

up to 40% of a hydrophilic component selected from the group consisting of a hydroxyalkane, a dihydroxyalkane, a polyethylene glycol having an average molecular weight of at most 1000, 1,2-propylene glycol, ethanol, and combinations thereof;

wherein the ~~said~~ preconcentrate, when mixed with ~~an aqueous medium selected from the group consisting of~~ water or simulated gastric fluid, gives an average droplet size of at most 10 microns, and ~~which upon oral administration of~~ a dose of the preconcentrate has a taxane bioavailability of ~~ranging from~~ 25% to 60% of the ~~said~~ taxane in the ~~said~~ dose upon oral administration.

30. (Amended) The ~~liquid~~ preconcentrate of claim 29, wherein the hydrophilic component comprises 1,2-propylene glycol and ethanol ~~are in combination~~.

34. (Amended) The ~~composition~~ preconcentrate of claim 29, wherein the preconcentrate also includes ~~further including~~ an inhibitor of P-glycoprotein transport system or an inhibitor of cytochrome P450 enzyme.

35. (Amended) The ~~composition~~ preconcentrate of claim 34, wherein the ~~inhibitor is~~ preconcentrate comprises grapefruit extract or a component thereof.

36. (Amended) The preconcentrate ~~composition~~ of claim 29, wherein the taxane is paclitaxel or docetaxel.

37. (Amended) A method of orally or parenterally administering a taxane to a subject in need of same comprising administering a dose of a storage-stable, self-emulsifying, and non-aqueous preconcentrate of a taxane consisting essentially of:

10 to 80% w/w of a hydrophobic component selected from the group consisting of a triglyceride, a diglyceride, a monoglyceride, a free fatty acid, a fatty acid ester, a fish oil, a vegetable oil, and combinations thereof;

20 to 80% w/w of a surfactant ~~phase~~ component ~~comprising at least~~ consisting of one or more non-ionic ~~surfactant~~ surfactants; and

up to 40% w/w of a hydrophilic component selected from the group consisting of a hydroxyalkane, a dihydroxyalkane, a polyethylene glycol having an average molecular weight of at most 1000, and combinations thereof;

wherein the ~~said~~ preconcentrate, when mixed with ~~an aqueous medium selected from the group consisting of~~ water or simulated gastric fluid, gives an average droplet size of at most 10 microns~~;~~ and ~~which upon oral administration of~~ a dose of the preconcentrate has a taxane bioavailability of ~~ranging from~~ 25~~%~~ to 60% of the ~~said~~ taxane in the ~~said~~ dose upon oral administration.

38. (Amended) The ~~A~~ method of claim 37, wherein the taxane is solubilized in the preconcentrate.

Claims 39-53 are new.